

Claims

1. A specific binding member which is specific for and binds directly to the ED-B oncofoetal domain of fibronectin (FN).

2. A specific binding member according to claim 1, which comprises an antibody antigen binding domain.

3. A specific binding member according to claim 2, wherein said antibody antigen binding domain is of human origin.

4. A specific binding member according to any one of claims 1 to 3, which binds to all FNs containing ED-B after treatment of the FN with the protease thermolysin.

5. A specific binding member according to any one of claims 1 to 4, which binds to all recombinant FNs containing type III homology repeats which include the ED-B domain.

6. A specific binding member according to any one of claims 1 to 5 whose binding to B-FN is inhibited by the ED-B domain.

7. A specific binding member according to any one of the preceding claims, which binds to B-FN from human, mouse, rat, chicken and any other species in which the ED-B domain is conserved.

8. A specific binding member according to any one of the preceding claims which binds to B-FN without treatment of the FN with N-glycanase.

9. A specific binding member according to any one of the preceding claims having a variable heavy (VH) chain region of the sequence derived from human germline DP47 (codon 1 Glu - codon 98 arg inclusive in Figure 1) and the CDR3 sequence Ser Leu Pro Lys.

[illegible]

10. A specific binding member according to any one of claims 1 to 8 having a variable heavy (VH) chain region of the sequence derived from human germline DP47 (codon 1 Glu - codon 98 Arg inclusive in Figure 1) and the CDR3 sequence Gly Val Gly Ala Phe Arg Pro Tyr Arg Lys His Glu.
11. A specific binding member according to any one of claims 1 to 8 having a variable light (VL) chain region of the sequence derived from human germline DPL16 (codon 1 Ser - codon 90 Ser inclusive in Figure 1) and the remainder of the CDR3 sequence as Pro Val Val Leu Asn Gly Val Val.
12. A specific binding member according to any one of claims 1 to 8 having a variable light (VL) chain region of the sequence derived from human germline DPL16 (codon 1 Ser - codon 90 Ser inclusive in Figure 1) and the remainder of the CDR3 sequence as Pro Phe Glu His Asn Leu Val Val.
13. A specific binding member according to any one of claims 1 to 8 having a variable heavy (VH) chain region of the sequence derived from human germline DP47 (codon 1 Glu - codon 98 Arg inclusive in Figure 1) and the CDR3 sequence.
14. A specific binding member according to any one of the preceding claims which, when measured as a purified monomer, has a dissociation constant (K_d) of 6×10^{-8} M or less for ED-B FN.
15. A specific binding member according to any one of the preceding claims, wherein said binding member comprises an scF₂ molecule.
16. A specific binding member of any one of the preceding claims, wherein said binding member comprises a dimeric scF₂ molecule.
17. A specific binding member of any one of the preceding

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claims, wherein said binding member comprises CGS-1 or CGS-2.

18. A pharmaceutical composition comprising a specific
5 binding member according to any one of the preceding claims
in an effective amount, in conjunction with a
pharmaceutically-acceptable excipient.

19. A nucleic acid that encodes a specific binding member
10 according to any one of claims 1 to 17.

20. A phage that encodes a specific binding member according
to any one of claims 1 to 17.

15 21. A host cell transformed or transfected with a nucleic
acid according to claim 19.

22. A specific binding member according to any one of claims
1 to 17 for use in therapy.

20 23. The use of a specific binding member according to any
one of claims 1 to 17 in the manufacture of a medicament for
the imaging or targeting of tumours.

25 24. A process for the production of a specific binding
member according to any one of claims 1 to 17, which process
comprises expression of a nucleic acid according to claim 19
in a host cell.

30 25. A process for the production of a specific binding
member according to any one of claims 1 to 17, which process
comprises:

35 a) screening a peptide or protein library expressed in
phage with recombinant antigen derived from the fibronectin
protein;

b) infecting host bacterial cells with positive clones;

c) subjecting positive phage clones to a process of

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affinity maturation;

d) repeating steps a) and b) to select positive phage clones with improved affinity for antigen;

e) infecting host cells with positive clones and
5 purifying antibody molecules from said host cells.

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26. The process of claim 25, wherein step a) comprises screening a scFv phage library with recombinant antigen derived from the fibronectin protein.

10 27. The process of claim 26, wherein said phage library expresses scFs of human origin.

15 28. The process of claim 23, wherein in step a), the phage clones are screened with recombinant antigens 7B89 or ED-B.

20 29. A diagnostic kit comprising a specific binding member according to any one of claims 1 to 17 and one or more reagents that allow the determination of the binding of said member to cells.

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add C3
add F1